

**REMARKS**

In response to the Office Action mailed June 22, 2009, Applicant respectfully requests reconsideration. Claims 13, 17-22, 25-27 and 54-56 were previously pending in this application and remain pending for examination, with claim 13 being independent. Claim 20 has been amended without prejudice or disclaimer to limit the recited promoter(s) to T7 promoter(s). No new matter has been added.

**Priority of Claim 20**

On page 4 of the Office Action, the Examiner stated that priority for claim 20 was granted only for the filing date of the parent of the instant application, US 09/347,311, filed on July 2, 1999. Applicant has amended claim 20 to remove the recitation of T3 and SP6 promoters. Accordingly, Applicant respectfully requests reconsideration of the priority benefit of claim 20, because the GB priority applications contain support for the T7 promoter.

**Rejections Under 35 U.S.C. § 102**

1. The Examiner maintained the rejection of claim 20 under 35 U.S.C. § 102(a) as allegedly anticipated by Fire et al. (WO 99/32619 A1, the "Fire PCT application"). The Examiner also maintained the rejection of claim 20 under 35 U.S.C. § 102(e) as allegedly anticipated by Fire et al. (US 6,506,559, the "Fire US patent"). Applicant respectfully requests reconsideration and withdrawal of both rejections.

Applicant has amended claim 20 such that it only recites T7 promoter(s). Accordingly, as noted above, claim 20 is entitled to the benefit of the GB priority applications. As such, neither the Fire PCT application nor the Fire US patent is prior art to claim 20.

Therefore, Applicant respectfully requests withdrawal of the rejection of claim 20 under 35 U.S.C. § 102(a) as allegedly anticipated by Fire et al. (WO 99/32619 A1) and under 35 U.S.C. § 102(e) as allegedly anticipated by Fire et al. (US 6,506,559).

2. The Examiner rejected claim 20 under 35 U.S.C. § 102(a) as being anticipated by Timmons et al. (Nature, 1998, 395:854, citation of record).

Applicant has amended claim 20 such that it only recites T7 promoter(s). Accordingly, as noted above, claim 20 is entitled to the benefit of the GB priority applications. As such, neither the Fire PCT application nor the Fire US patent is prior art to claim 20.

Therefore, Applicant respectfully requests withdrawal of the rejection of claim 20 under 35 U.S.C. § 102(a) as being anticipated by Timmons et al.

3. The Examiner rejected claims 13, 18, 21, 25 and 55 under 35 U.S.C. § 102(a) as being anticipated by Timmons et al. (East Coast Worm Meeting Abstract 180). The Examiner contends that Timmons et al. teaches feeding of *C. elegans* with bacteria that express dsRNA from a myo3 promoter and that the dsRNA down-regulates target gene expression/activity in the *C. elegans*. The Examiner asserts that “[s]ince the bacteria comprising a ‘myo3:dsRNA’ construct successfully transcribes and thereby expresses the dsRNA in the bacteria, and since Timmons et al. perform the active steps of the claimed methods, it inherently and logically flows that the bacteria organism fed to *C. elegans* must be adapted to express a transcription factor that participates in transcribing or expressing the promoter-flanked dsRNA such as GFP dsRNA or unc22 dsRNA, absent evidence to the contrary.” (emphasis added)

Applicant respectfully disagrees that the Examiner has met the Office’s burden for showing anticipation of the claimed invention by Timmons et al., either explicitly or inherently. The Examiner’s statements include assumptions about the content and public availability that are

unsupported and unwarranted. There is nothing in Timmons et al. that describes the claimed method, including that the recited expression vector comprises a promoter or promoters flanking the DNA sequence. As a result, Timmons et al. does not teach each and every element of the claimed invention, and therefore does not anticipate the claimed invention.

First, Applicant respectfully disagrees that Timmons et al. teaches the following and submits that there is no proof offered by the Examiner for the following: (1) that Timmons et al. teaches successful transcription and expression of dsRNA in the same way as claimed by Applicant; (2) that Timmons et al. used myo3 promoter to express dsRNA; and (3) that the bacteria of Timmons et al. is adapted to express a transcription factor as recited in the claims.

(1) Timmons et al. does not teach successful transcription and expression of dsRNA as is claimed by Applicant. In fact, Timmons et al. is silent as to the way in which dsRNA was expressed other than a minimal reference to the genes (GFP, unc-22) that were the basis for the undefined dsRNA sequences. It is clear that Timmons et al. in no way describes what Applicant claims – “an expression vector that comprises a DNA sequence corresponding to the gene of interest, in which said expression vector comprises a promoter or promoters flanking said DNA sequence such that the promoter or promoters initiate transcription of said DNA sequence to produce double stranded RNA upon binding of a transcription factor to said promoter or promoters”. In contrast, the extent of Timmons et al.’s specific teaching of dsRNA expression is the following sentence: “Bacteria expressing GFP or unc-22 dsRNA were fed to myo3::GFP worms on standard NGM plates.”

(2) Timmons et al. does not described using a myo3 promoter to express dsRNA. Contrary to Examiner’s statement on page 5 of the Office Action that “Since bacteria comprising a ‘myo3:dsRNA’ construct...”, the only thing that Timmons et al. appears to teach is that GFP is expressed in *C. elegans* using a myo3 promoter (“...myo3::GFP worms consistently express a high level of GFP in muscle...”). In fact, Timmons et al. is entirely silent as to the promoter or promoters used to express GFP dsRNA or the promoter or promoters used to express unc22 dsRNA.

Moreover, it does not make sense that Timmons et al. would have used the myo3 promoter, which is active in *C. elegans* muscle, to drive expression of dsRNA. This is because the dsRNA is allegedly expressed in the bacteria fed to the *C. elegans* by Timmons et al., and not in the *C. elegans* itself; and there is no teaching that the myo3 promoter is active in bacteria.

(3) The Examiner states on page 5 of the Office Action that “it inherently and logically flows that the bacteria organism fed to *C. elegans* must be adapted to express a transcription factor that participates in transcribing or expressing the promoter-flanked dsRNA....” Applicant respectfully disagrees with this statement that appears to be directed to claim 21, which recites a method in which a micro-organism is adapted to express a transcription factor.

For inherent anticipation, it is the Examiner’s burden to show that the features of the claimed invention are necessarily present in the prior art. For inherent anticipation, an invention must be a necessary result of the prior art, not a probability or possibility. **Error! Hyperlink reference not valid.**Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1269 (Fed. Cir. 1991)(“Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.” The theory of inherent anticipation serves to accommodate “situations where the common knowledge of technologists is not recorded in the reference; that is, where technological facts are known to those in the field of the invention, albeit not known to judges.”). Moreover, an invitation to investigate is not an inherent disclosure. See Corning Glass Works v. Sumitomo Elec. U.S.A., Inc., 868 F.2d 1251, 1262 (Fed. Cir. 1989).

Second, Applicant respectfully disagrees that the Examiner has adequately shown the requisite public accessibility of the Timmons et al. prior art reference. Public accessibility determines whether a reference constitutes a printed publication for purposes of anticipation. In re Hall, 781 F.2d 897, 898-899 (Fed. Cir. 1986). A reference is publicly accessible “upon a satisfactory showing that such document has been disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art exercising reasonable diligence,

can locate it . . . .” SRI Int'l, Inc. v. Internet Sec. Sys. Inc., 511 F.3d 1186, 1194 (Fed. Cir. 2008) (quoting Bruckelmyer v. Ground Heaters, Inc., 445 F.3d 1374, 1378 (Fed. Cir. 2006)).

As noted by the Examiner, Applicant cited the Timmons et al. abstract and indicated a date of May 12, 1998. Applicant does not concede, however, that the Timmons et al. abstract was publicly accessible and available as of that date or any date prior to the filing date of Applicant's earliest priority application. The date noted in the Information Disclosure Statement citing Timmons et al. was a date provided by a third party that filed third party observations in connection with a corresponding European application. Because Applicant was obliged to provide the Timmons et al. reference to the USPTO under the duty of disclosure requirements, including the date alleged by the third party, Applicant did so. However, Applicant in no way concedes that May 12, 1998 is the date that the Timmons et al. abstract was publicly available. As stated in the Information Disclosure Statement, providing the information was not an admission that the information is, or is considered to be, in fact, prior art as defined by 35 U.S.C. § 102.

The initial burden of proof for showing public availability is the Examiner's. The “mere existence” of a reference would not be viewed by a court as prima facie evidence that the reference was available prior to Applicant's critical date. In re Richard S. Lister, No. 2009-1060, slip op. at 17 (Fed. Cir. September 22, 2009). As noted above, the date provided in Applicant's IDS is that alleged in third party observations in connection with a corresponding European application.

Therefore, Applicant respectfully requests withdrawal of the rejection of claims 13, 18, 21, 25 and 55 under 35 U.S.C. §102(a) as being anticipated by Timmons et al.

### **Rejections Under 35 U.S.C. § 103**

The Examiner rejected claims 13, 17-22, 25-27 and 54-56 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Timmons et al. (East Coast Worm Meeting Abstract 180) in

view of Raftery et al. (Diagnostic Molecular Pathology: The American Journal of Surgical Pathology, 1993, 2:120-1245), Wang et al. (Gene, 1991, 100:195-199), Vanfleteren (Experientia, 1976, 32:1087-1088), and Talkad et al. (Journal of Bacteriology, 1978, 135:528-541, citation of record). Applicant respectfully traverses the rejection.

In rejecting the claims as obvious, the Examiner repeated the erroneous characterization of the Timmons et al. reference as described above in the response to the anticipation rejection based on Timmons et al. Applicant respectfully disagrees that Timmons et al. teaches the following and submits that there is no proof offered by the Examiner for the following: (1) that Timmons et al. teaches successful transcription and expression of dsRNA in the same way as claimed by Applicant; (2) that Timmons et al. used a myo3 promoter to express dsRNA; and (3) that the bacteria of Timmons et al. is adapted to express a transcription factor as recited in the claims. A full description of the deficiencies of Timmons et al. is provided above.

Additionally, the rejection of the claims as obvious must fail for the reason that the claimed feature must be present in the prior art references. As stated in MPEP 2141.02.V., “Obviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established.”, citing In re Rijckaert, 9 F.2d 1531, 28 USPQ2d 1955 (Fed. Cir. 1993). Here, there is no teaching in Timmons et al. that the bacteria fed to *C. elegans* comprises an expression vector that comprises a promoter or promoters flanking a DNA sequence corresponding to the gene of interest such that the promoter or promoters initiate transcription of the DNA sequence to produce double stranded RNA upon binding of a transcription factor to said promoter or promoters.

Moreover, the Examiner must provide a sufficient showing that the allegedly inherent feature is necessarily present in the cited prior art. As stated in MPEP 2112.IV., “In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art.” Citing Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd.

Pat. App. & Inter. 1990) (emphasis in original). The Examiner has not provided the required basis as is described above.

As such, Applicant submits that the cited combination of references does not include all of the elements of the claimed invention, and therefore the Examiner has not met the burden of the Patent Office for unpatentability of the claimed invention as obvious over the cited combination of references..

Finally, the claimed invention is not a “predictable” or “identified” solution to a problem as was found in KSR Int’l Co. v. Teleflex Inc., 550 U.S. 398 (2007), for the substitution of an electronic linkage for a mechanical linkage. In KSR, the court found that there were “design incentives and other market forces” that might prompt variations, which, if predictable in type and in implementation by a person of ordinary skill in the art, might render a claim obvious. Here there is no market force or other driver that would have prompted a person of skill in the art to make the claimed invention.

Applicant also asserts, based on the opinion of Dr. Erwin Sablon (see previously filed Declaration of Erwin Sablon at ¶17; copies of the Declaration and Exhibit 1 are enclosed), that the person of skill in the art would not have had a reasonable expectation of success of practicing the invention claimed in the present application, by using the type of vectors known in the art to express double stranded RNA “inside” a microorganism, feeding such a microorganism that expresses the double stranded RNA (“inside” its cell wall) to *C. elegans*, and exerting an effect, from the inner content of the bacterium towards the cell cytoplasm of *C. elegans* cells. Thus, the predictability aspect required by the court in KSR also is missing from the prior art cited by the Examiner. For this additional reason, Applicant submits that the claims are not obvious over the cited combination of references.

Therefore, Applicant respectfully requests withdrawal of the rejection of claims 13, 17-22, 25-27 and 54-56 under 35 U.S.C. § 103(a) as obvious.

**Double Patenting Rejection**

1. Claims 13, 17-22, 25-26 and 54-56 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 8-16 and 20-22 of U.S. Patent 7,005,423. Applicant respectfully disagrees that the claims of US 7,005,423 render obvious claims 13, 17-22, 25-26 and 54-56. However, to facilitate allowance of the instant claims, Applicant files herewith a terminal disclaimer over US 7,005,423.

Accordingly, withdrawal of the double patenting rejection of claims 13, 17-22, 25-26 and 54-56 is respectfully requested.

2. Claims 13, 17-22, 25-26 and 54 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 41-46 of copending Application No. 12/055,607 (“US 12/055,607”). Applicant respectfully traverses the rejection.

Patentably distinct features of the claimed invention in US 12/055,607 include the following features of the recited DNA construct used in the methods claimed in US 12/055,607:

- 1) an inter-promoter region positioned downstream of the 3’ end of a first promoter and downstream of the 3’ end of a second promoter;
- 2) at least one cloning site positioned in the inter-promoter region; and
- 3) at least one first transcription terminator, positioned, as seen from the 3’ end of the first promoter, downstream of the first promoter and downstream of the at least one cloning site, wherein the at least one first transcription terminator is operably linked to the first promoter, and
- 4) at least one second transcription terminator positioned (as seen from the 3’ end of the second promoter) downstream of the second promoter and downstream of the at least one cloning site, wherein the at least one second transcription terminator is operably linked to the second promoter.



Applicant respectfully disagrees that it would have been obvious to omit all of the inter-promoter region, cloning site, at least one first transcription terminator and (optionally) at least one second transcription terminator in order to obtain the claimed invention. Moreover, the Examiner provides no reason for making such modifications to the claims of US 12/055,607. The Examiner merely suggests that the claims are obvious because both sets of claims are drawn to methods for down-regulating gene expression using dsRNA in *C. elegans* by feeding *E. coli* “comprising two promoters”. With respect, and as noted above, the claims of US 12/055,607 and the claims of the instant application differs in several ways that render the claims patentably distinct. The Examiner has not provided any other reason why a skilled person would have been motivated and had a reasonable expectation of success in making the claimed invention. Therefore Applicant respectfully traverses the rejection and requests its withdrawal.

Moreover, Applicant notes that the rejection is a provisional rejection. In the event that the rejection is not withdrawn, Applicant may file a terminal disclaimer when the claims are otherwise in allowable format (See MPEP § 804).

**CONCLUSION**

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below to discuss any outstanding issues relating to the allowability of the application.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. D0590.70011US00.

Dated: December 22, 2009

Respectfully submitted,

By: /John R. Van Amsterdam/  
John R. Van Amsterdam  
Registration No.: 40,212  
WOLF, GREENFIELD & SACKS, P.C.  
Federal Reserve Plaza  
600 Atlantic Avenue  
Boston, Massachusetts 02210-2206  
617.646.8000

**X12/22/09X**